Impact of control measures on malaria transmission and general mortality *

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This paper is an attempt to relate modifications observed in general and infant mortality rates with the dynamic changes in transmission induced by malaria control measures. The observations indicated relationships between the efficacy of control and a decrease in mortality. The daily parasitological inoculation rate was reduced from 0.00958 infective bites per individual before treatment to 0.00037 after treatment (a decrease of 96%). In two years, general mortality decreased from 23.9 to 13.5 deaths per 1000 population and infant mortality decreased from 157 to 93 per 1000 live births. This indirect benefit of malaria control deserves attention in a wider assessment of measures directed against vector-borne diseases.

A research project of the World Health Organization was carried out in Kenya from 1972 to 1976 to evaluate the impact of fenitrothion [a] spraying on malaria transmission. In addition to the usual field data collected on entomology and malaria parasitology, information on vital events and migration movements was also periodically registered as a routine. This study is a modest attempt to relate the modifications observed in the general mortality with the changes induced on the dynamics of malaria transmission by the attack measures against the vectors of the disease.

MATERIAL

The project was located in Kenya, Nyanza Province, west of Kisumu Town in a rural hilly area of about 200 km² on the shores of Lake Victoria. Malaria prevalence is of the hyper-holoendemic type. *Plasmodium falciparum* is the dominant malaria parasite species and *P. malariae* is quite frequent. *P. ovale* and *P. vivax* are seldom encountered. The malaria vectors *Anopheles gambiae* (species A and B) and *A. funestus* are both prevalent throughout the area.

To satisfy the requirements of the experimental design, the territory was divided into three zones (see Fig. 1): the evaluation zone (treated area), with a population of 17 000; the comparison zone (untreated area), with a population of 3800; and the barrier zone, with a population of 32 000. The role of the latter zone was merely to protect the population of the evaluation zone against reintroduction of the insect vectors and therefore will not be discussed in the present study.

Fenitrothion (wettable dispersible powder, 40% formulation) was used as the only intervention measure in the evaluation and barrier zones. The insecticide was applied inside dwellings at a fixed dosage of 2 grams (technical product) per square metre for 8 rounds at intervals of 3 months; the first coverage of the treated area was completed in August 1973 and the last in June 1975.

Starting one year prior to the application of fenitrothion, epidemiological and demographic data were regularly collected in both the evaluation and comparison zones at monthly house-to-house visits: in particular, blood smears were systematically taken from all infants and examined for the presence of malaria parasites, and vital events and popu-

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[a] Organophosphorus insecticide with residual effect.

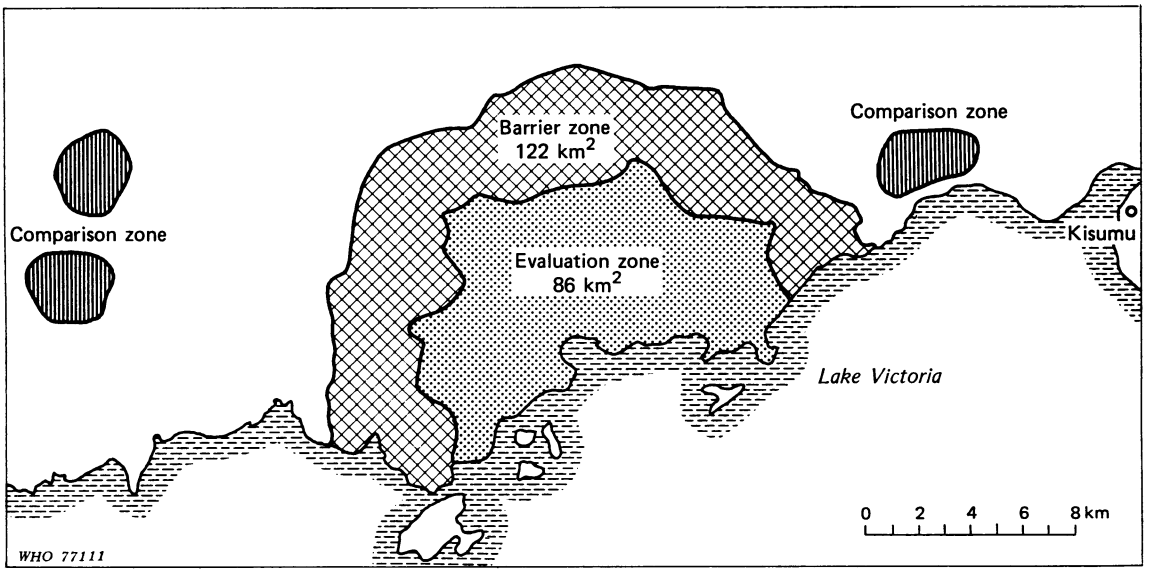

Fig. 1. Impact of malaria control measures: trial area, Nyanza Province, Kenya.

lation movements—births, deaths, immigrants (newcomers), and emigrants (persons absent for more than 3 months)—that had occurred during the previous month were recorded.

During the first house-to-house visit in September 1972, a census registration form was completed for each family and thereafter kept up to date at subsequent visits. Persons were considered as resident if they were present at the time of the visit or away from the house but not outside the treated area. Those who were absent from the area were, however, kept on the resident file for 3 months, after which time they were considered as emigrants and excluded from the resident population.

METHOD

Evaluation of the impact of fenitrothion spraying on malaria transmission was based on comparison of the malaria force of infection in the treated and untreated zones. This parameter, which is an expression of the parasitological inoculation rate, was estimated from the rate of acquisition of the infection during the first year of life. The method of estimation makes use of the simple epidemiological model developed by Muench (*1*) and has already been described by Pull & Grab (*2*).

To estimate the rate of decrease of the general mortality and its new level in the treated zone, a negative exponential function with movable asymptote was adjusted to the observations. Under the assumption that malaria was mainly responsible for the mortality difference between treated and untreated zones and that malaria fatality is proportional to the existing amount of infection, the observed daily decrease should be comparable to the daily natural malaria cure rate. This hypothesis was tested with reference to the first standard for interruption of malaria transmission [a] set up by the WHO Expert Committee on Malaria (*3*).

RESULTS

Malaria transmission

Early each month, any new-born infants were examined for the presence of malaria parasites in the blood and were followed up longitudinally every month until they were found positive or until they reached the age of one year. Aggregated findings and derived age-specific incidence rates are given in the first three columns of Table 1 for the treated area and of Table 2 for the untreated area. Up to

[a] This standard reads: " Successive parasite rates taken in any age group of the population over the age of three years should decline progressively in 12 months to a value which can be shown with statistical confidence to be less than 22% of the original value and which ideally should approximate 16% of that value ".

Table 1. Observed and simulated age-cumulated incidence rates derived from results of monthly blood examination of susceptible infants followed up in the treated area, October 1973–September 1975

Age group (days)	No. of susceptible infants examined	No. of primary infections	Monthly parasite incidence rate (%)	No. of susceptible infants [a] in a cohort of 1000	Calculated new cases in the cohort	Age-cumulated incidence rate (%)	
						calculated from observations	simulated with model
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
10–29	694 [b]	2	0.29	1000	3	0.3	0.4
30–59	887	1	0.11	997	1	0.4	1.3
60–89	741	5	0.67	996	7	1.1	2.4
90–119	587	5	0.85	989	8	1.9	3.5
120–149	464	5	1.08	981	11	3.0	4.5
150–179	384	5	1.30	970	13	4.3	5.6
180–209	298	9	3.02	957	29	7.2	6.6
210–239	234	3	1.28	928	12	8.4	7.6
240–269	189	4	2.12	916	19	10.3	8.7
270–299	168	6	3.57	897	32	13.5	9.7
300–329	121	1	0.83	865	7	14.2	10.7
330–359	93	0	0.00	858	0	14.2	11.7

[a] At the beginning of each age-class.
[b] Estimated as two-thirds of the number of infants under one month, under the assumption of a 10-day incubation period.

Table 2. Observed and simulated age-cumulated incidence rates derived from results of monthly blood examination of susceptible infants followed up in the untreated area, September 1972–September 1975

Age group (in days)	No. of susceptible infants examined	No. of primary infections	Monthly parasite incidence rate (%)	No. of susceptible infants [a] in a cohort of 1000	Calculated new cases in the cohort	Age-cumulated incidence rate (%)	
						calculated from observations	simulated with model
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
10–29	526 [b]	21	4.0	1000	40	4.0	9.1
30–59	590	108	18.3	960	176	21.6	28.5
60–89	417	109	26.1	784	205	42.1	46.4
90–119	278	102	36.7	579	212	63.3	59.8
120–149	182	49	26.9	367	99	73.2	69.8
150–179	134	44	32.8	268	88	82.0	77.3
180–209	92	28	30.4	180	55	87.5	83.0
210–239	65	16	24.6	125	31	90.6	87.3
240–269	46	10	21.7	94	20	92.6	90.4
270–299	41	10	24.4	74	18	94.4	92.8
300–329	30	12	40.0	56	22	96.6	94.6
330–359	15	4	26.7	34	9	97.5	96.0

[a] At the beginning of each age-class.
[b] Estimated as two-thirds of the number of infants under one month, under the assumption of a 10-day incubation period.

the start of the spraying operations, in September 1973, no distinction was made between the two areas and global data for the pre-operation phase are given in Table 2.

To estimate the rate of acquisition of the infection by susceptible infants, the age-cumulated incidence rates of new malaria cases were first calculated for an initial cohort of 1000 new-born infants on the basis of the observed age-specific parasite rates given in column 3 of Tables 1 and 2. The intermediate steps are shown in columns 4 and 5 and the resulting age-cumulated incidence rates in column 6.

Under the assumption that the infant population is exposed to a constant force of infection, the acquisition of the disease in a cohort of susceptible new-born infants can be simulated by the equation:

$$y=1-\exp(-ht) \quad (1)$$

which is the solution of the differential equation of the simple Muench model (*1*), and where y is the age-cumulated incidence rate, t the age in days, and h the daily rate of inoculation per susceptible infant.

Applying the method described by Muench (*1*) to the rates that would have been observed in the cohort (column 6 of Tables 1 and 2), the estimated values obtained for h were 0.00037 in the treated area and 0.00958 in the untreated area. The equations of the simple epidemiological model thus become respectively:

$$y=1-\exp(-0.00037t) \quad (2)$$

for the treated area and

$$y=1-\exp(0.00958t) \quad (3)$$

for the untreated area.

The theoretical cumulated incidence rates calculated from these equations are given for the mid-point of the successive age classes in the last column of Tables 1 and 2.

Both the observed and the theoretical age curves of acquisition of infection are presented in Fig. 2. As already noted by Pull & Grab (*2*), the hypothesis of a constant force of infection is not fully confirmed by the facts: it seems that the risk of inoculation reaches its maximum value around the age of 3 months in the absence of antivector measures and around the age of 6 months when insecticide is sprayed. No simple explanation for this phenomenon can be offered here. On the whole, however, the observed and the theoretical lines do not diverge significantly and the model estimated inoculation rates can be considered as reflecting satisfactorily the prevailing force of infection in the two areas.

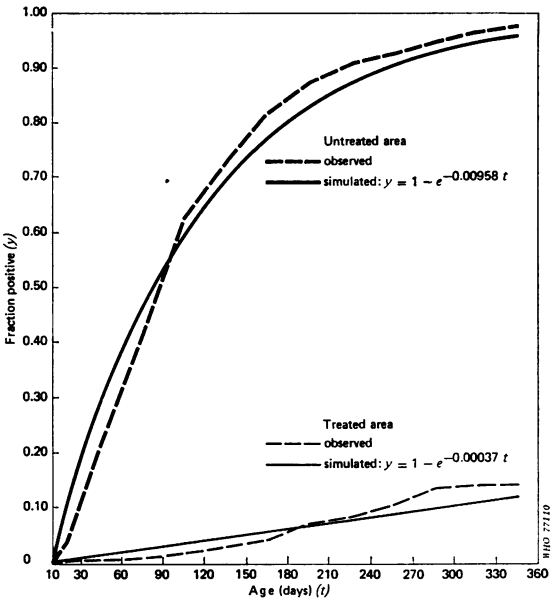

Fig. 2. Age-cumulated incidence of malaria detected by microscopic examination in the treated and untreated areas (observed and simulated curves).

General mortality

Demographic data collected each month were consolidated for annual periods centred on the date of the first spraying round (August 1973). The large amount of migratory movement can be appreciated from the summary results presented in Tables 3 and 4 for the treated and the untreated areas, respectively; it should be noted, however, that in many instances the same persons appear in both columns 4 and 5 of these tables, since absences of more than 3 months but less than one year are not infrequent among seasonal workers.

In the untreated area the average birth rate was 32.0 per 1000 population over the 3-year period considered, while the corresponding average crude death rate was 24.5.

In the evaluation area, the pre-operational baseline birth rate was somewhat lower than expected (26.2 per 1000 population, compared with 32.0 in the control area), levelling to rates comparable to those observed in the control area for the 2 years following the start of the attack phase (see column 8

Table 3. General vital statistics and movement of population in the treated area, August 1972–August 1975[a]

Period	Resident population	Vital events and migration in successive 12-month periods				Annual balance	Mid-period population	Annual birth rate per 1000 population	Annual death rate per 1000 population
		births	deaths	immigrants	emigrants				
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
August 1972	17 109								
		469	428	5592	4045	+ 1588	17 903	26.2	23.9
August 1973	18 697								
		586	291	4887	6176	- 994	18 200	32.2	16.0
August 1974	17 703								
		575	247	4376	3442	+ 1262	18 334	31.4	13.5
August 1975	18 965								

[a] The first round of insecticide spraying took place in August 1973.

Table 4. General vital statistics and movement of population in the untreated area, August 1972–August 1975

Period	Resident population	Vital events and migration in successive 12-month periods				Annual balance	Mid-period population	Annual birth rate per 1000 population	Annual death rate per 1000 population
		births	deaths	immigrants	emigrants				
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
August 1972	3635								
		118	86	823	730	+ 125	3698	31.9	23.3
August 1973	3760								
		101	98	853	759	+ 97	3809	26.5	25.7
August 1974	3857								
		143	93	858	999	- 91	3812	37.5	24.4
August 1975	3766								

of Tables 3 and 4); it would therefore not be justified, on the present evidence, to interpret the apparent increase in the birth rate as an indirect benefit from the considerable reduction in malaria transmission achieved by the spraying operations.

The situation is different with regard to the general mortality. As shown in the last column of Table 3, the crude death rate recorded in the treated area during the pre-operational year (23.9 per 1000 population) was comparable to the average rate measured in the control area (24.5), whereas the rates observed in the 2 years following the start of the spraying compaign reveal a drastic decrease (33.1% after one year and 43.5% after 2 years).

As shown in the previous section, the attack measures against the malaria vectors have reduced the daily inoculation rate to less than 4% of its original value. When the transmission of malaria is completely interrupted, the amount of infection in the population will decrease at the average rate of natural recovery. On the basis of follow-up data collected by Earle et al. (*4*), a value of 0.005 was deduced by Macdonald (*5*) for the daily recovery rate of *P. falciparum* infection. The decrease in the parasite rate referred to in the first standard of interruption of malaria transmission is indeed based on this value.

Under the hypothesis of constant fatality rates, it could be assumed as a first approximation that the mortality from malaria and other diseases whose transmission may be reduced by insecticide spraying will similarly decrease at a constant average daily rate.

The crude death rate will ultimately stabilize itself at a new level reflecting the mortality from all other causes. The corresponding dynamics of the current crude death rate m_t can be expressed quantitatively by the simple mathematical relationship:

$$m_t = (m_o - m_L) \exp(-kt) + m_L \qquad (4)$$

where m_o and m_L are, respectively, the initial and the asymptotic final annual crude rates, and k is the constant rate of decrease of the mortality component affected by spraying operations. For comparability purposes, the time t will be measured in days and k will therefore be a daily rate.

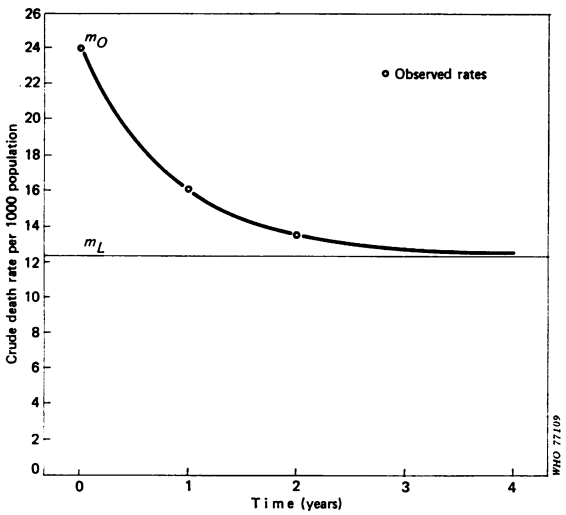

Fig. 3. Onserved and simulated changes in general mortality after malaria control measures were instituted.

Numerical values are calculated for these parameters by constraining function (4) to reproduce for three consecutive years the death rates displayed in column 9 of Table 3 and repeated in the first column of Table 5. The resultant expression of the equation is:

$$m_t = 11.6 \exp(-0.00315t) + 12.3 \qquad (4')$$

Thus the initial death rate of 23.9 per 1000 population will be reduced by 11.6 at a constant daily rate of 0.00315 to reach ultimately the asymptotic new mortality level of 12.3 (see Fig. 3). This final rate is 48.5% lower than the initial rate, while the decrease observed over the first two years was 43.5%.

Columns 3 and 4 of Table 5 show respectively the actual and relative time change of the mortality component apparently affected by the intervention, i.e., the mortality in excess of the expected new level (12.3 per 1000 population).

The pattern of decrease in malaria prevalence that theoretically would be observed if the transmission of infection were completely interrupted is displayed in the last column of Table 5: the parasite rate would be reduced to less than 1% of its initial value after 3 years, while after the same time the above-mentioned mortality component will still be over 3% of its initial value, as seen in column 4 of the same table. In the previous section, however, it was demonstrated that a residual transmission of malaria still prevailed in the treated area. As long ago as 1916, Ross (*6*) had already demonstrated that, when the inoculation rate h and the recovery rate r are constant, the limiting parasite rate is estimated by the ratio $h/h+r$. With the numerical values calculated for h (0.00037) [a] and adopted for r (0.005), the malaria prevalence rate should finally stabilize itself at a rate of 6.9%. Since the observed parasite rate was 58.1% in March 1973, 32.1% in March 1974, and 19.8% in March 1975, it is clear that

[a] This rate was calculated on observations made during a period of rapid change in the parasite load of the population and could be an over-estimate of its value at the end of the period, leading similarly to a slightly over-estimated limiting parasite rate.

Table 5. Analysis of observed and simulated changes in general mortality

Year	Total crude death rate per 1000 population		Mortality component affected by intervention		Theoretical relative decrease of malaria prevalence [a] in %
	observed	simulated [b]	death rate [c]	relative decrease in %	
	(1)	(2)	(3)	(4)	(5)
0	23.9	23.9	11.6	100	100
1	16.0	16.0	3.7	31.9	16.0
2	13.5	13.5	1.2	10.3	2.6
3	—	12.7	0.37	3.2	0.42
4	—	12.4	0.12	1.0	0.07

[a] Based on the first standard for the interruption of malaria transmission.
[b] Calculated with the equation $m_t = 11.6\exp(-0.00315t) + 12.3$.
[c] Excess of simulated rate over m_L.

attack measures made a relatively faster impact on the affected mortality component than on morbidity.

Infant mortality

As the infants were examined each month, it was possible to record by age the infant deaths occurring at successive monthly intervals. The data on the number of infants seen and the number of deaths registered at each monthly visit were aggregated by age for the survey period and are presented in columns 1 to 4 of Table 6. Cumulated infant deaths were then calculated for a theoretical cohort of 1000 live-born infants, by applying to the successive survivors the age-specific death rates derived from the observed mortality. The results of the computation are shown in columns 5 and 6 of Table 6 for the treated and untreated areas, respectively. They have also been plotted on Fig. 4, in which the age profiles of infant mortality are more easily appreciated and compared.

The protective effect of maternal antibodies is clearly demonstrated by the relatively low level of mortality under the age of 3 months observed in the untreated area. As a matter of fact, the same force of mortality prevailed in the treated area up to this age, but Fig. 4 shows also that the impact of the spraying operations on the mortality of older

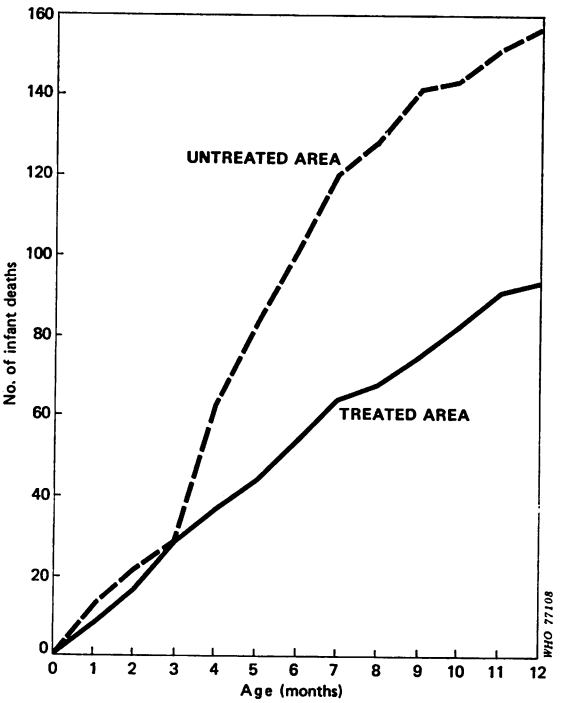

Fig. 4. Age-cumulated infant deaths in theoretical cohorts of 1000 live-born infants.

Table 6. Infant mortality by age, according to areas

Age group (months)	Treated area, 1973–75, Aggregated No. of:		Untreated area, 1972–75. Aggregated No. of:		Age-cumulated infant deaths [a] in a cohort of 1000 new-born infants	
	infants seen	deaths recorded	infants seen	deaths recorded	treated area	untreated area
	(1)	(2)	(3)	(4)	(5)	(6)
0	518	4	521	6	8	12
1	514	5	515	5	17	21
2	509	6	510	4	29	29
3	503	4	506	18	37	63
4	499	4	488	11	44	84
5	495	5	477	9	54	102
6	490	5	468	10	64	121
7	485	2	458	4	68	129
8	483	4	454	7	75	142
9	479	4	447	1	83	144
10	475	4	446	4	91	152
11	471	1	442	3	93	157

[a] At the end of each age-class.

infants can hardly be denied. In the treated area, the force of mortality was practically kept at constant rates throughout the first 12 months of life, while in the untreated area infants over 3 months of age were exposed to an increasing risk of death.

For the whole first year of life, the mean infant death rate calculated with the data collected during the survey period was 93 per 1000 live-born infants in the treated area and 157 per 1000 in the untreated area (see columns 5 and 6 of Table 6).

It should also be noted that, out of the 48 infants who died in the treated area, only two (4.2%) had demonstrated malaria parasites in the blood, whereas in the untreated area 53.7% of the 82 infants who died had malaria parasites in the blood prior to death. The corresponding average parasite rates [a] for the infant population in the survey period were 1.8% and 35.6%, respectively.

DISCUSSION AND CONCLUSIONS

The efficacy of insecticide spraying on malaria transmission was clearly demonstrated by the findings: the daily inoculation rate dropped from 0.00958 before treatment to 0.00037 after treatment (a decrease of 96%), and the general parasite rate, which was initially close to 60% in both the treated and untreated areas, went down to approximately 20% after 2 years of control in the former, the calculated long-term asymptotic limit being 6.9% under the assumption that the inoculation and recovery rates would remain stable.

A spectacular indirect benefit was recorded in the general mortality. The annual crude death rate decreased from 23.9 to 13.5 per 1000 population in 2 years (a reduction of 10.4 per 1000 population). The mortality component affected by the attack measures was calculated as 11.6 annual deaths per 100 population (the estimated asymptotic final level being 12.3); the reduction observed after 2 years therefore corresponded practically to 90% of this component $100 \times 10.4/11.6$).

[a] The parasite rate was estimated four times a year. In the treated area, only data from infants born after the start of the spraying operations were analysed.

A similar computation for the malaria parasite rate shows that, for the same period, the observed absolute decrease was 38.3 positive per 100 persons examined (from 58.1 to 19.8), while the expected ultimate decrease was 51.2 positive per 100 examined (from 58.1 to 6.9), thus indicating a 75% decrease only of the infection load assumed to be affected by the intervention.

Similar observations regarding the relatively faster impact of attack measures on mortality than on morbidity had already been made by Gramiccia & Hempel (*7*).

Estimated age profiles of infant deaths in the treated and untreated areas showed the definite protective effect of maternal antibodies during the first 3 months of life. On the other hand, the total infant death rate calculated for cohorts of 1000 newborn infants reflected, beyond doubt, the impact of vector control measures on the survival of older infants, since a reduction of 40.8% was observed in this rate (from 157 to 93 deaths per 1000 respectively in the unprotected and protected areas).

The effect of the reduction in malaria transmission on the parasite rate in infants is clearly demonstrated by the contrast between the mean infection prevalence in the two areas: 35.6% of infants positive for parasitaemia in the untreated area, against only 1.8% positive in the treated area (a reduction of 94.9%). Relatively, much higher parasite rates were observed prior to death in both areas among infants who died under one year of age (53.7% and 4.2%, respectively, in the untreated and treated areas), which indicates the role of malaria infection as a factor contributing to the increased risk of death among infants with parasitaemia.

Although the scope of the survey was limited in space and time, the observations made clearly indicated a relationship between the efficacy of antivectorial measures (as reflected by the reduction of the inoculation rate) and the decrease in both general mortality and infant mortality. This additional indirect benefit, already noted by Bruce-Chwatt et al. (*8*), deserves particular attention in the wider assessment of control measures against specific vector-borne diseases.

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RÉSUMÉ

EFFET DES MESURES ANTIPALUDIQUES SUR LA TRANSMISSION DU PALUDISME ET SUR LA MORTALITÉ GÉNÉRALE

Un projet de recherches a été effectué au Kenya par l'Organisation Mondiale de la Santé de 1972 à 1976. Le but de ces recherches était de mesurer l'effet des applications intradomiciliaires de fénitrothion sur la transmission du paludisme. Vu l'absence de statistiques démographiques relatives à la population de la zone d'étude, il apparût nécessaire d'enregistrer périodiquement les événements vitaux et les mouvements migratoires.

Cette étude ne veut qu'essayer d'établir un rapport entre les changements observés dans les taux de mortalité générale et infantile avec les modifications dynamiques de la transmission du paludisme provoquées par les mesures de lutte appliquées contre les vecteurs de la maladie.

Nonobstant la portée restreinte de ce travail, aussi bien dans le temps que dans l'espace, les observations tendent à prouver qu'il existe un rapport évident entre l'efficacité des mesures de lutte et la réduction des taux de mortalité. L'efficacité des opérations insecticides est prouvée par la réduction du taux journalier parasitologique d'inoculation qui passa de 0.00958 piqûres infectantes par personne avant tout traitement à 0.00037 après traitement (une réduction de 96%). La mortalité générale décrût en deux ans de 23.9 à 13.5 pour mille habitants — soit une réduction de 43.5%. De même, la mortalité infantile a été réduite de 157 à 93 décès pour mille enfants — soit une réduction de 40.8%.

Le bénéfice additionnel et indirect des opérations antipaludiques que constitue la diminution de la mortalité a été rarement mesuré et mérite une attention toute particulière dans le cadre d'une évaluation plus complète des mesures de lutte contre les maladies transmises par des insectes vecteurs.

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